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EXPERIMENTAL MEASLES IN RABBITS AND MONKEYS

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In our search of the literature on experimental measles we have been unable to find any mention of attempts having been made to transmit the virus to rabbits. Anderson and Goldberger¹ speak of the apparent insusceptibility of animals other than the monkey to the inoculation of measles virus, but no reference is given.

In order to test the receptivity of rabbits to the infection of measles, the blood of 6 patients with measles was inoculated into 6 rabbits. Three of the rabbits were inoculated with blood drawn on the second day, 2 rabbits with blood drawn on the third and 1 with blood drawn on the fourth day after the onset of the disease. In all we inoculated 17 rabbits, 6 with human blood and 11 with the blood of rabbits that had given evidence of a reaction. The inoculations were given intravenously in amounts varying from 1 to 15 cc. All of the rabbits inoculated with human blood gave evidence of a reaction. So also did all but 2 of the rabbits subinoculated from these 6 rabbits. Passage inoculations for subsequent injections into monkeys were carried out only from patient "S."

SYMPTOMS IN RABBITS

Fifteen rabbits developed symptoms in from 3 to 7 days. The symptoms were not so marked as in monkeys. In some instances there was a rise in temperature coincident with a decrease in the total leukocyte count, but this was by no means constant. We noted also that in the majority of the rabbits there was frequently a leukocytosis on the second, third or fourth day after injection followed by a decrease in the total leukocyte count. The fact that these findings were not constant, together with the fact that we had found great fluctuations in the daily counts of these animals for one week prior to their inoculation, led us to disregard these changes in the white blood counts.

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¹ U. S. Public Health Reports, 1911, 26, p. 847.

Of the 15 rabbits showing symptoms of measles, 10 developed small hyperemic, slightly elevated spots on the labial mucosa; in 5 instances these spots showed whitish centers. Twelve rabbits developed in from 2 to 4 days, a marked conjunctivitis with a moderate edema of the lids and lachrimation. Four rabbits developed a slight diarrhea.

In from 3 to 8 days all of the 15 animals showed erythema of varying degrees, from a slight flush over the chest and in the axillary region to a general redness extending to the groin. A redness of the skin always followed the shaving of the rabbits, but, unlike the control animals noted in the following, the flush became more intense in from 3 to 8 days.

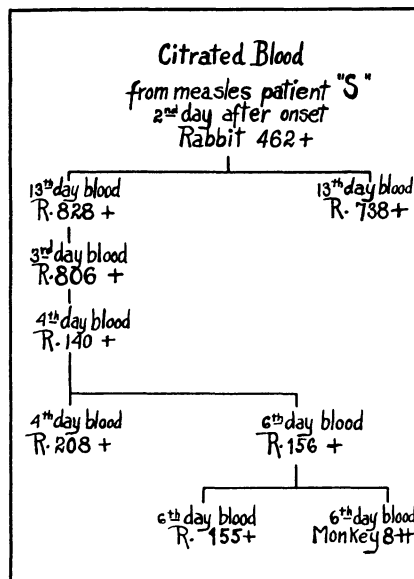
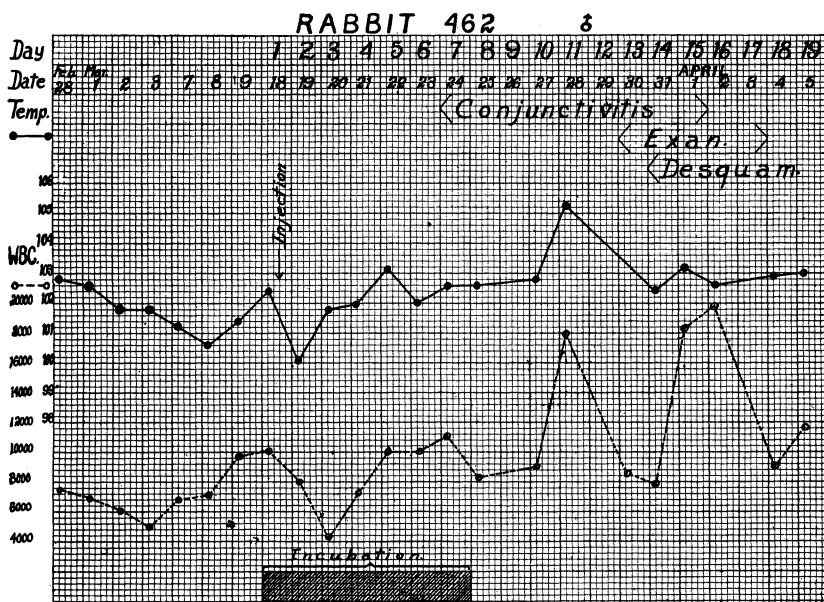


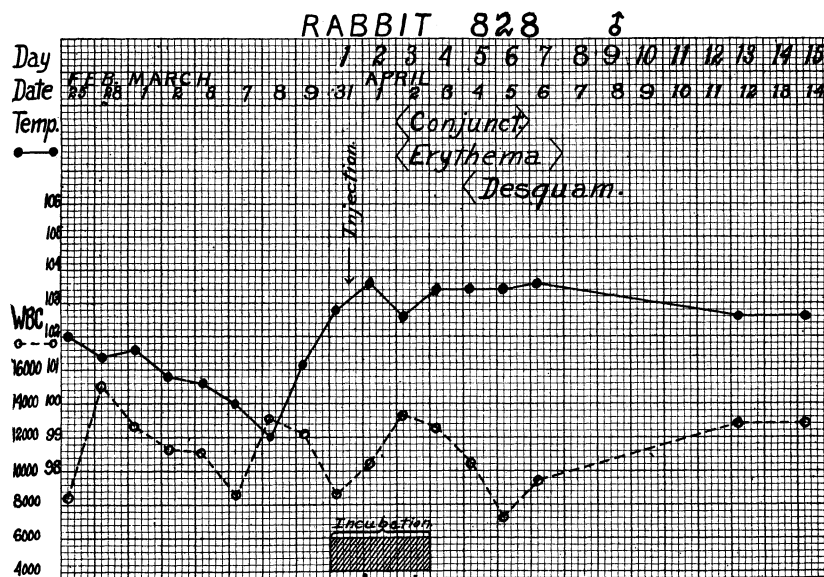
Chart 1.—Transmission of measles virus from case "S" through 5 rabbits to a monkey; suggestive reaction +, typical measles reaction ++.

In no instance was a distinctly typical exanthem noted. In 8 rabbits we noted several erythematous macules on the chest and abdomen. Such a rash was not distinctive. Neither is the reaction on the skin of rabbits after inoculation with cowpox vaccine the typical one that takes place in human beings.

In all of the 15 rabbits a marked desquamation occurred, beginning from the fifth to the fourteenth day. Both the shaved and unshaved portions of the neck, chest, axillae, abdomen and groin were involved.



A



B

Chart 2.—Transmission of measles virus, strain from case "S," by means of intravenous inoculation of whole citrated blood; A, rabbit 462 from case "S"; B, rabbit 828 from rabbit 462.

In two instances the desquamation was fine and branny; with the remaining 13 animals large flake-like scaling took place.

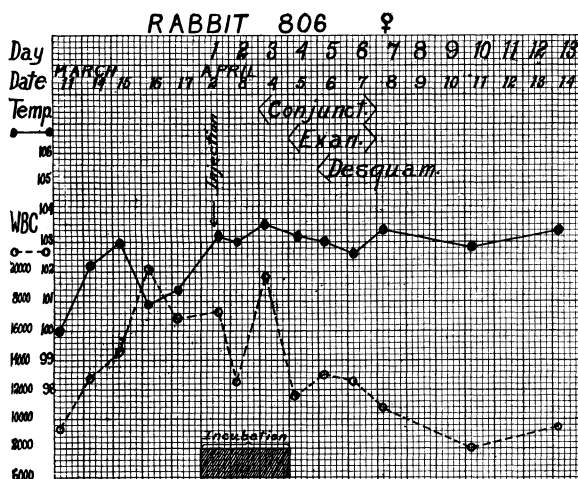
From one of the human cases, "S," the virus was passed through 5 rabbits (Charts 1, 2 and 3). On the sixth day after inoculation, the fifth rabbit was bled from the heart and the citrated blood injected intravenously into monkey 8, *M. rhesus*. The monkey developed a leukopenia in 3 days (Chart 4A). On the fourth day there was loss of appetite, slight reddening of the eyelids and lacrimation with a marked erythema over the face, neck and shoulders, while on the labial mucosa two discrete, elevated, hyperemic macules with bluish white centers appeared. On the fifth day a maculopapular rash appeared about the mouth, cheeks and forehead. On the sixth day, over the bluish abdomen of the monkey, small clusters of yellowish, elevated papules appeared. From the sixth to the ninth day there was a moderate erythematous, granular rash on the mucous membrane of the lips. The papules on the labial mucosa disappeared on the eighth day. The rash also began to fade and marked desquamation was noted on the face, chest, shoulders, abdomen and in the groin.

Blake and Trask² have shown that monkeys inoculated intratracheally with nasopharyngeal washings from patients with measles develop characteristic symptoms of measles. Accordingly, we reinoculated monkey 8, *M. rhesus*, one month later with nasopharyngeal washings containing another strain of measles virus (case "O"). The monkey failed to react (Chart 4B). The control (monkey 24, *M. rhesus*, chart 5A) developed the characteristic symptoms of measles in 6 days.

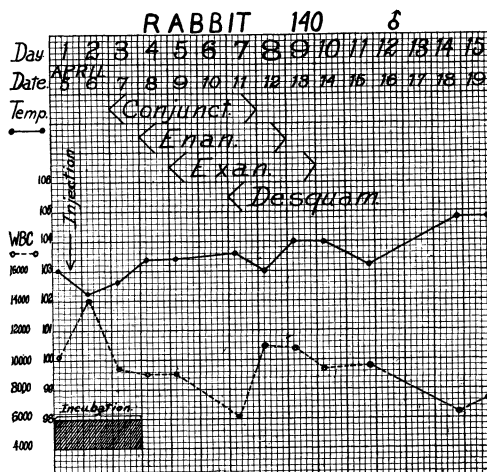
In order to test the receptivity of the monkey to the infection of measles with blood from a human being with measles the following experiment was made:

Two patients with measles, "Y" and "O," were bled on the third day after the onset of the disease. In both cases Koplik spots were present. Conjunctivitis and coryza were present in one case only. Both cases showed a maculopapular rash. The citrated blood of these two patients was pooled and 10 cc were inoculated intravenously within an hour into monkey 26, *M. rhesus* (chart 5B). On the fourth day after inoculation the animal was drowsy; loss of appetite was noted, and the diminution in the total leukocyte count was marked. The monkey developed no distinct symptoms until the sixth day when a few bright red spots, slightly elevated, were noted on the labial mucosa. On the seventh day discrete, slightly raised, hyperemic macules with

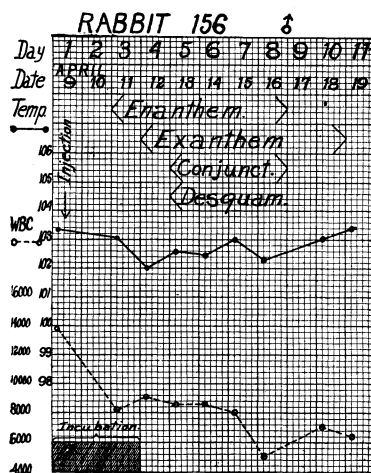
² Jour. Exper. Med., 1921, 33, p. 385.



A



B



C

Chart 3.—Transmission of measles virus strain from case "S" by means of intravenous inoculation of whole citrated blood; A, rabbit 806 from rabbit 828; B, rabbit 140 from rabbit 806; C, rabbit 156 from rabbit 140.

bluish white centers were present on the inside of the cheeks; the enanthem on the labial mucosa was more marked but not coalescent. On the eighth day we noted a few flat reddish macules, disappearing under pressure, on the face and shoulders. Conjunctivitis appeared on the ninth day; the lids were thickened and hyperemia and lacrimation were present. The following day the exanthem had spread to the chest and abdomen, while the rash on the face of the monkey showed a yellowish brown pigmentation. During the next 4 days the exanthem gradually faded, the spots on the chest and abdomen becoming a yellowish brown also. Desquamation started on the eighth day, but was never marked. By the fourteenth day the animal appeared well; the

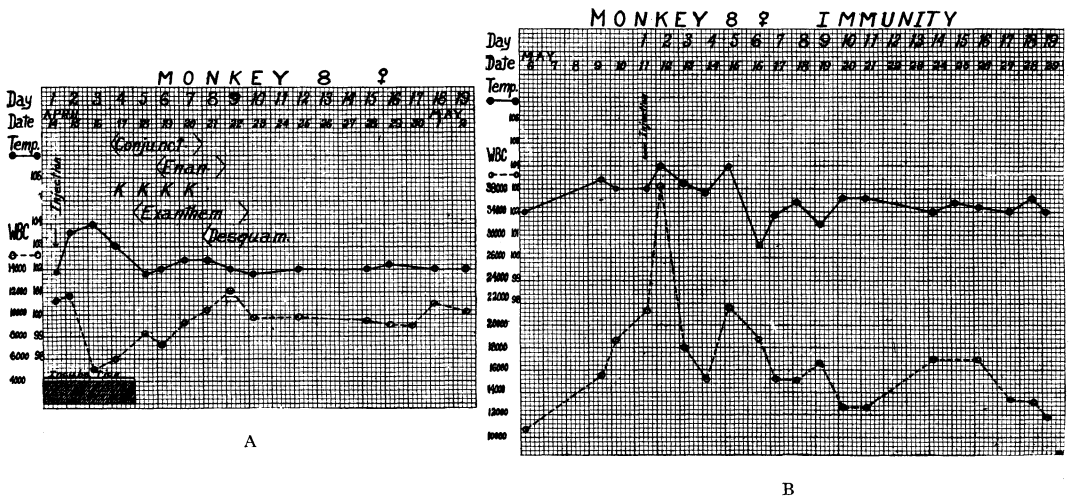
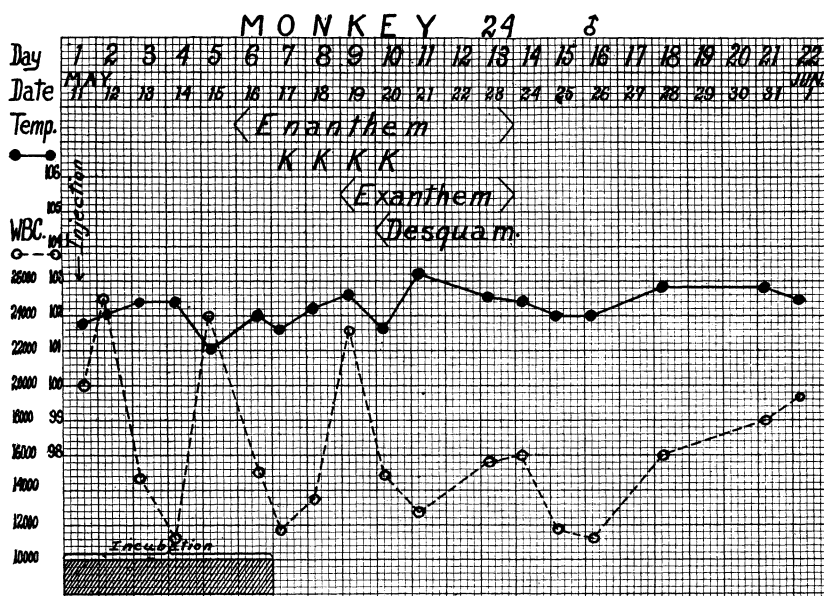


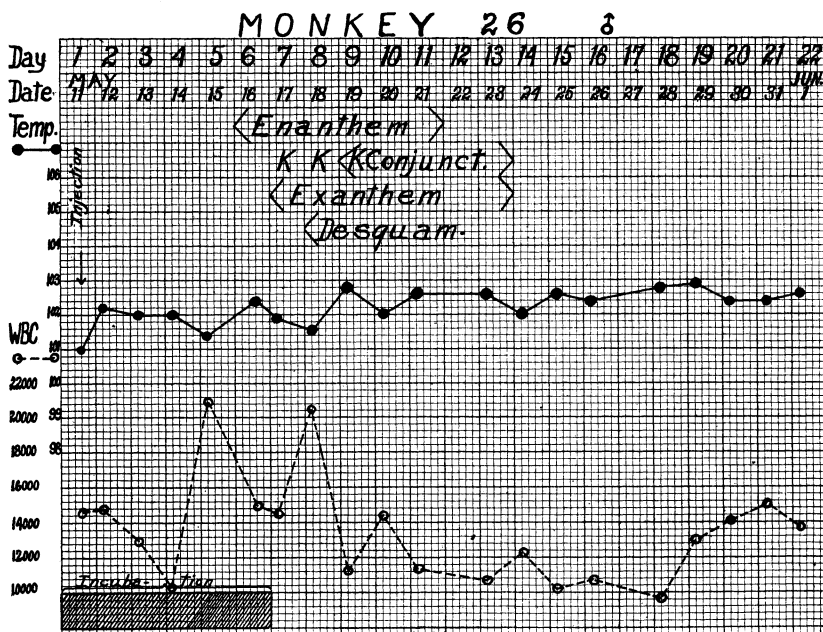
Chart 4.—Observations on monkey 8; A, transmission of measles virus strain from case "S" by means of intravenous inoculation of whole citrated blood from rabbit 156 (chart 3C); B, attempted reinfection by means of intratracheal inoculation with 10 c.c. of nasopharyngeal washings containing another strain of measles virus (case "O"). The rise in the total leukocyte count prior to inoculation was due, in all probability, to a slight diarrhea. This condition rapidly ceased on change of food. As Blake and Trask have noted, the sharp rise following the injection of nasopharyngeal washings is probably due to the effect of other organisms. This animal showed no reaction to the virus and was discharged on the nineteenth day. Control monkey 24 (chart 5A), inoculated with 10 c.c. of the same washings developed the characteristic symptoms of measles in 6 days.

exanthem had entirely faded and only a slight pigmentation and desquamation were noted.

Controls.—Eleven rabbits were shaved over the neck, chest, axillae, abdomen and groin. Six rabbits were inoculated intravenously each with 5 cc of citrated blood as follows: two with blood from two cases of diphtheria, one from a case of lobar pneumonia, one from a case of lethargic encephalitis, one with normal human blood and one with normal



A



B

Chart 5.—A, observations on monkey 24 inoculated intratracheally with 10 c.c. of nasopharyngeal washings from case "O"; B, observations on monkey 26 inoculated with 10 c.c. of whole citrated pooled blood from measles patients "Y" and "O".

rabbit blood. The total leukocyte count of all these rabbits showed considerable variation from day to day with the exception of the rabbit inoculated with normal rabbit blood. This count remained fairly constant.

The 5 uninoculated rabbits were kept under observation for the appearance of an erythema and desquamation. All of the 11 control animals showed a redness of the skin incident to shaving. This flush disappeared in from 48 to 72 hours, whereas in the animals showing evidence of a reaction to the inoculation of blood from patients with measles, the redness became more marked from the third to the eighth day following the inoculation and persisted for from 3 to 5 days and then gradually faded. In no instance was desquamation noted in the 11 control rabbits.

Microscopic examination of scrapings made from the spots on the labial mucosa showed no parasitic invasion.

Aerobic and anaerobic cultures made of blood prior to inoculation showed no evidence of growth.

SUMMARY

Blood from 6 patients with measles was inoculated into rabbits. The animals gave evidence of infection.

Passage from one human case of measles was carried on through 5 rabbits, and a monkey inoculated with the blood of the fifth rabbit gave typical symptoms of measles.

A monkey inoculated with pooled blood from two human cases of measles taken on the third day after the onset of the disease gave the characteristic symptoms of measles.

Blood from cases other than measles when inoculated into rabbits failed to give evidence of infection.